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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,653	01/22/2005	Oleg Iliich Epshtein		8593

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
04/02/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/522,653	EPSHTEIN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5* is/are pending in the application.

4a) Of the above claim(s) *4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and amendments received January 9, 2008 are acknowledged.

Claims 1-3 have been amended.

Claims 4 and 5 stand withdrawn from consideration as being drawn to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03, for reasons of record set forth in the restriction requirement mailed February 22, 2007.

Claims 1-3 are under examination in the instant office action.

The declaration of inventor Oleg I. Epshtein under 37 CFR 1.132 is acknowledged and will be discussed with the rejections of record to which it is addressed.

Information Disclosure Statement

2. Applicant's IDS received March 14, 2008 is acknowledged and has been considered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been obviated by applicant's claim amendments received January 9, 2008 which remove the recitation of the terms and phrases discussed in the rejection of record .

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-3 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sinha (US patent 6,379,669, of record) in view of Davenas et al. (of record), in view of Epshtein et al. (of record), and in view of Feldman et al. (US Patent 5,741,488, of record).

The office action mailed July 9, 2007 states:

> Sinha teaches antibodies to prostate-specific antigen (PSA) and their methods of production (see entire document, particularly the abstract and columns 7 and 8). These antibodies are taught as being present in compositions for use in methods of treatment (see particularly column 9).
>
> These teachings differ from the instant claimed invention in that the antibodies in the compositions of Sinha are not disclosed as having been made by multiple consecutive dilutions and exposure to external factors.
>
> Davenas et al. teach very low concentrations (i.e. ultra low) of anti-IgE antibodies produced by repeated serial dilutions and exposure to the external factor of mixing by using a vortex (see entire document, particularly page 816 and the legend of Fig. 1). These antibodies maintain their ability to induce a physiological response, measured by the basophil degranulation, even at such low concentrations (see particularly the abstract, figure 1, and Tables 1-3).
>
> Epshtein et al. teach that potentiated antiserum when administered in very low doses causes measurable biological responses in vivo (see entire document, particularly the abstract).
>
> Feldman et al. teach that antibody based therapies are expensive and that lower doses of antibodies offer the advantage of lower financial costs to the patient (see entire document, particularly lines 20-25 of column 3).
>
> Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make compositions comprising very low doses of anti-PSA antibodies. Motivation to do so comes from the teachings of Sinha that his anti-PSA antibodies are to be used for methods of treatment, the teachings of Feldman et al. that low doses of antibody result in lower financial costs to patients, and the teachings of Davenas et al. and Epshtein et al. that very low doses of antibody maintain

biological activity. As such, the skilled artisan would be able to make a biologically effective medicament that would impose less financial costs on patients. A person of ordinary skill in the art would have a reasonable expectation of success in making and using such compositions based upon the two distinct model systems of Davenas et al. and Epshtein et al., both of which disclose that antibody solutions maintain biological activity even when highly diluted.

Further, the courts have held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). See MPEP § 2144.05. Note that in the instant situation, the general conditions are disclosed by Sinha and identifying optimum or workable ranges for dilutions of the antibodies disclosed by Sinha requires only routine skill in the art.

Applicant's arguments filed January 9, 2008 have been fully considered but they are not persuasive. Applicant first argues that the rejection is improper because these is no motivation to combine the references and that there is no expectation of success in doing so. Specifically, applicant alleges that neither Sinha nor Feldman et al. disclose homeopathic dilutions, and that neither Davenas et al. nor Epshtein et al. disclose medicaments, particularly medicaments comprising anti-PSA antibodies. Applicant continues that none of the references "discloses a medicament effective for treating prostate disease comprised of homeopathic dilutions."

This argument is not persuasive. Applicant has pointed out why the cited art does not anticipate the claimed invention. Such an analysis does not speak to the question of obviousness. The instant claimed invention is a composition comprising diluted anti-PSA antibody. Anti-PSA antibodies were known in the art (Sinha) as were motivations for diluting antibodies (reduced cost as per Feldman et al.). Further, the art provides clear working examples of antibodies used in homeopathic dilutions (Davenas et al. and Epshtein et al.). Therefore, a person of ordinary skill in the art would have been motivated to make the claimed compositions at the time the invention was made because homeopathic dilutions use very low concentrations of antibody and thus would have a low cost. Applicant's argument that a person of ordinary skill in the art would not have a reasonable expectation of success in making the claimed compositions is not persuasive because working examples of homeopathic dilutions of antibodies were known in the art (Davenas et al. and Epshtein et al.) and because as applicant argues on page 5 of the response received January 9, 2008 "Homeopathic dilutions and homeopathic technology have been known in the filed of homeopathy in the US to anyone of average skill in that filed for almost 200 years". As such it appears

unreasonable that a person of ordinary skill in the art would not have a motivation for or a reasonable expectation of success in diluting antibodies. As for applicant's contention that the claimed homeopathic compositions are not taught for treating a prostate disease, applicant is reminded that such a recitation provides for an intended use of the claimed product, and such intended use limitations are accorded patentable weight only when they serve to change the structure of the claimed product. In the instant case, the claimed product is diluted anti-PSA antibodies as discussed above and the recitation of "effective in treating a prostate disease" does not alter the structure of the claimed product.

Applicant's second argument is that the claimed products are not obvious due to commercial success, with applicant pointing to the declaration of inventor Oleg I. Epshtein to support this argument.

The argument of commercial success is not persuasive. First, evidence of commercial success must be commensurate in scope with the claims. The declaration discusses sales of IMPase, which appears to be a homeopathic dilution of a specific anti-PSA antibody made using precise numbers and types of dilution steps. The instant claimed products encompass one or more generic homeopathic dilutions. As such, the species of IMPase does not support the claimed genus of compositions. Second, to be persuasive an argument of commercial success must show explicit sales results that demonstrate evidence of market share, including such things as total sales for competing products in the market, the differences between these competing products and applicant's product, total sales for products embodying the invention, pricing of the various products, information on advertising within relevant markets and any other information relevant to the inquiry. In other words, applicant must establish a nexus between the claimed features and the commercial success. As such, commercial success, if it exists, cannot be derived from other factors such as heavy promotion, advertising or brand name recognition. Note that gross sales figures do not show commercial success absent evidence as to market share. See *Cable Electric Products, Inc. v. Genmark, Inc.* 770 F.2d 1025, 226 USPQ 881 (Fed. Cir. 1985). In the instant declaration, inventor Epshtein discloses that:

"The medicament IMPase (ultra-low doses to a prostate specific antigen) - is some of the top 20 selling medicaments in the over-the-counter segment of the market. From the start of the production I0 million doses of IMPase have been manufactured and sold. The medicament is on of the leading export product from Russia to Ukraine and Kazakhstan." (page 3 of declaration).

However, this data is irrelevant since the OTC market encompasses medicaments for all sorts of unrelated diseases and disorders, including such things as aspirin for headaches. What is needed is a comparison to other medicaments used to treat prostate disease. Further, how long has production been going on? How has it been determined that IMPase is "a leading export product"? What is the relevance of any of this to the sales of other prostate disease medicaments? In summary, it appears that the declaration of inventor Oleg I. Epshtein et al. fails to establish the required nexus between alleged commercial success and the instant claimed product.

Further, it should be noted that a strong case of obviousness may be established such that the objective evidence of nonobviousness is not sufficient to outweigh the evidence of obviousness. See MPEP 716.01(d).

The rejection is maintained.

6. No claims are allowable.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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